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NosoSim: an agent-based model of nosocomial pathogens circulation in hospitals

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Abstract

Over the last decades, nosocomial infections have become a major Public Health problem in hospitals worldwide. In this context, it is very important to understand the underlying mechanisms of nosocomial pathogen transmission, in order to devise and assess the best control strategies. Here, we present an agent-based model of pathogen transmission in a hospital ward, NosoSim. In this model, the actions of patients and health-care workers are reproduced at all times in a spatially explicit environment, and pathogen colonization and transmission are simulated. NosoSim allows users to define simulation parameters such as: ward geography, including -but not limited to- the number of rooms; daily allocation and schedule of all present healthcare workers; patient status; microbiological and epidemiological characteristics of all circulating pathogens. After describing the model and its implementation, we illustrate its potential applications through an example addressing a real-life Public-health issue. In this application, NosoSim is used to assess the factors which promote so-called "super-spreading events" in hospital settings.

Keywords: hospital; agent-based modeling; nosocomial infections; MRSA; VRE

1. Introduction

Although not a recent problem, nosocomial infections have reemerged as a major Public Health issue worldwide over the last decades [1]. One of the main reasons for this phenomenon is that nosocomial pathogens have become increasingly resistant to antibiotic treatment. Some bacteria, such as vancomycin-resistant enterococci (VRE),

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vancomycin-intermediate and vancomycin-resistant *Staphylococcus aureus* (VISA and VRSA), and multi-drug resistant *Pseudomonas aeruginosa*, are now resistant to almost all commercially available antibiotics and have confronted physicians with the possibility of a post antibiotic era [2].

In that context, it is of the utmost importance to gain better understanding of the mechanisms of pathogen transmission in hospitals, as well as to be able to evaluate various control strategies. Computer modeling can help identify factors responsible for observed patterns of occurrence. It also provides qualitative and quantitative predictions that help understand transmission dynamics and give rise to criteria for the assessment of interventions.

Over the last 10 years, several mathematical models have been developed for studying health-care-associated pathogens [3]. They broached a wide array of issues, including the assessment of control strategies such as antibiotic prescribing policies [4], rapid detection and isolation strategies [5] or various hygiene measures [6], as well as the importance of patient re-admission and moves between the general community and several health-care institutions [7,8]. Most of these models were compartmental models, which aggregate patient and health-care worker (HCW) populations into compartments such as colonized or uncolonized patients and contaminated or uncontaminated HCWs. Compartmental models assume behavioral homogeneity inside compartments and homogeneous mixing between individuals [9].

Agent-based models (ABMs), in contrast, view patients and HCWs as individual agents, and can therefore simulate the heterogeneity of patient and HCW behavior. ABMs have been used extensively in the last decade to simulate financial markets, car traffic, customer behavior in a supermarket or pedestrian movements such as those in relation with a panic phenomenon [10]. They are well suited for modeling complex biological phenomena, including the spread of infectious agents, because they account for stochasticity and for individual variations, as well as easily integrate time and space heterogeneity [10-12]. In hospital settings, they allow for an explicit description of individual daily schedules and moves of HCWs, as well as of individual characteristics of patients such as immune status or drug exposure, and of specific procedures performed during visits of a given patient by a given HCW.

Here, we present an agent-based model of pathogen transmission in a geographically realistic hospital ward, NosoSim (Nosocomial pathogens Simulation). The actions of human agents (patients and HCWs) are reproduced at all times, as well as pathogen colonization and transmission. After describing the model and its implementation, we illustrate its potential applications through an example. In this example, NosoSim was used to assess the impact of HCW profile on their potential to be responsible for super-spreading events associated with nosocomial pathogens.

2. The NosoSim model

NosoSim includes two types of agents: human agents (patients and HCWs) and biological agents (pathogens and antibiotics). For patients, key model parameters include the length of stay in the ward and the required care level during their hospital stay. Several organizational variables are defined for HCWs. Key parameters for pathogens are their transmissibility, the duration of human colonization and that of the conferred immunity.

2.1. Ward organization

2.1.1. Geographical description

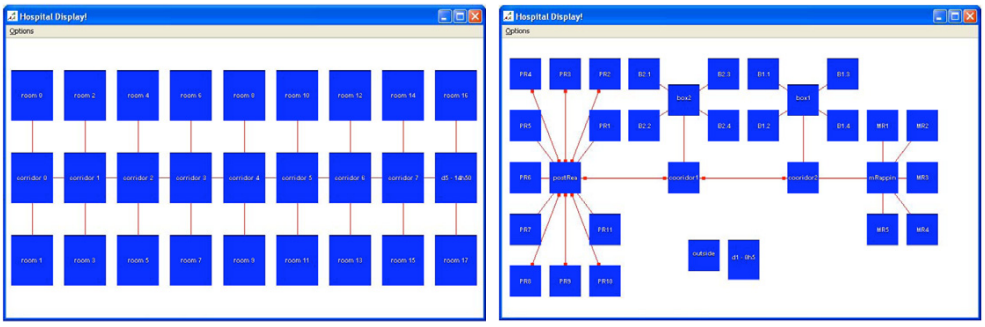

Fig. 1 (a) “Corridor” hospital ward; (b) “Mondor-like” hospital ward

2.1.2. Health-care workers (HCWs): distribution, schedule and allocation

The model includes some level of cohorting, meaning that a given number of patients (or patient rooms) are allocated to each HCW. All HCWs included in a simulation have a profile, which determines their daily timetable, and the duration and nature (in terms of time spent in direct contact) of their patient visits.

For each HCW profile present in the ward, the HCW to patient ratio is entered as a parameter. For instance, it is possible to define a ”nurse” profile, according to which ”nurses” will work 8 hours shifts, with a 2:1 patient to nurse ratio and 3 visits to each allocated patient per day, 60% of which is spent in direct contact. Table 1 depicts three examples of HCW profiles as an illustration.

Table 1. Three HCW profiles for NosoSim: “nurses”, “physicians” and “peripatetic HCWs.

HCW profile	Presence in the ICU	Number of patient visits	Duration of patient visits	Risk level of contacts	Number of patients assigned
Nurse	7 AM–7 PM	2	3 visits/day	1.5	2 patients
Physician	9 AM – 6 PM	4	1 visit/day	1	6 patients
Peripatetic HCW	9 AM – 6 PM	6	1 visit/day	1	all patients

2.2. Patients

This version of NosoSim simulates an ICU-like hospital ward where patients do not move from the room they are allocated, except for entering or leaving the ward. Rooms are supposed to be single. Only patient/HCW interactions are modeled; in particular, HCW/HCW interactions are not modeled yet.

2.3. Pathogen colonization and transmission

The model allows for the simulation of one or several pathogens in the hospital ward. Because colonization is the driving force behind many nosocomial epidemics, we chose to simulate colonization, rather than infection. Colonization may be (and often is) asymptomatic; symptoms, when they occur, are not explicitely modeled.

2.3.1. Colonization of patients

Patients may be colonized with any of the pathogens that are supposed to circulate in the ward. For each simulation, users may either select circulating pathogens from a built-in library, or define a new pathogen. For each pathogen, the duration of colonization is entered, as well as the transmissibility and the duration of natural immunity following decolonization.

Patients may either enter the ward already colonized or acquire colonization while they are in the ward. Colonization is transmitted from a patient to another via the hands of HCWs. During all patient-HCW contacts, there is a chance of colonization transmission; the transmission rate per minute of contact depends on the involved pathogen as well as on the profile of the HCW. However, the probability of patient-to-HCW transmission is the same as that of HCW-to-patient transmission.

Additional routes of transmission (e.g. airborne transmission) are not modeled in this version of NosoSim.

2.3.2. Colonization of HCWs

HCWs may be transiently colonized (hand carriage) with any of the pathogens that are supposed to circulate in the ward. The duration of this transient colonization is provided for each pathogen. No immunity period follows the end of transient colonization. HCWs acquire colonization from patients and may transmit the pathogen they are

carrying to other patients during their visits.

2.3.3. Competition between strains and multiple colonization

In simulations where several pathogens co-circulate in the ward, the model allows for multiple colonization. The ability of two pathogens to co-colonize an individual is defined by a crossed immunity parameter which is entered for all circulating pathogens. This parameter determines the level of protection against acquisition of a second pathogen in already colonized individuals; it works as a multiplying factor between 0 and 1, which is applied to the transmission probability.

2.4. Control measures

Various interventions may be implemented in NosoSim.

2.4.1. Antibiotic exposure

Antibiotics may be prescribed to patients, independently of their colonization status. Users can select one or several antibiotics from a built-in library. For each antibiotic, a mean duration of prescription is entered, as well a frequency of exposure in the hospital ward. Patients to which an antibiotic is prescribed are drawn at random among all unexposed patients each morning, in order to maintain the user-defined frequency of exposure to this antibiotic in the ward.

Bacterial pathogens may be affected by antibiotic exposure. For each circulating bacterial strain and each antibiotic, a level of sensitivity is entered. This sensitivity determines the probability of decolonization following antibiotic exposure.

2.4.2. Hand hygiene

HCWs may wash or rub their hands following patient contacts. In that case, hand hygiene will remove hand carriage with a given efficacy.

2.5. Model outcomes

2.5.1. Graphical outcomes

During simulations, pathogen circulation can be followed in real-time from a schematic representation of the hospital ward including all human agents with their location and colonization status. The prevalence of carriage among patients and HCWs is also depicted in real-time for each circulating pathogen. After simulations, a graphical representation of the chain of transmission provides a summary of events for each circulating pathogen.

2.5.2. Other outcomes

Several outcomes are routinely available using NosoSim, including carriage prevalence and incidence as a function of time for each circulating pathogen. What's more, it is rather straightforward to add other simple outcomes to NosoSim, provided that they are built from monitored entries such as colonization transmissions and acquisition or point prevalence.

2.6. Implementation

NosoSim is developed using the agent modeling toolkit RepastJ, the java implementation of Repast3 (http://repast.sourceforge.net/repast_3/). The java language was chosen for its interoperability, allowing the application to run (and be developed) under Windows XP and Mac OS X. It should also work under any java 5.0 equipped operating system. The project uses the JDOM API for handling XML and Apache Derby as relational

database management system.

A free executable version of NosoSim is downloadable from the project web site: http://sites.google.com/site/NosoSim/. The only requirement to run the project is to have a Java Runtime Environment version 5.0 (or higher) installed. The JDOM and Derby jars are included in the project files.

3. Application example

In this section, we illustrate potential applications of NosoSim through an example [13].

3.1. Background

Epidemiological data show that many nosocomial outbreaks seem to exhibit "super-spreading events," where relatively few individuals are responsible for a large part of epidemic transmissions. The underlying mechanisms of super-spreading remain unclear and may involve a combination of host, pathogen, and environmental effects. However, increased transmission is bound to be correlated with host activities and behavior, such as hygiene practices, frequency of bodily contacts, tendency to seek treatment, and compliance with control measures.

In this application, we examine the conditions under which individual noncompliance to hygiene measures among HCWs may lead to super-spreading of nosocomial pathogens in a hospital ward. Using the NosoSim model, we investigate the impact of HCW profile (in terms of daily allocation and schedule and nature of patient contacts) on their super-spreading capacity.

3.2. Model parameters

This application was carried out in the context of an 18-bed "corridor"-type ICU (Figure 1), with 90% bed occupancy, and a mean length of stay of 10 days. Three HCW profiles were included in the ward:

(i) Two assigned HCW profiles (AP), the first assigned HCW profile -typically a nurse- involving frequent contacts with a limited number of patients and the second assigned HCW profile -typically a physician- involving fewer contacts but with more patients.

(ii) One "peripatetic HCW" profile, involving a single daily contact with all patients -for instance a therapist or a radiologist.

Each AP HCW was assigned to a specific subpopulation of patients, while peripatetic HCWs were in contact with all patients. During his or her shift, each HCW made a fixed number of visits to each patient in his or her specified population. For example, a nurse had 3 daily contacts with 2 different patients. Characteristics of HCW profiles and their daily schedule and allocation are reported in Table 1.

3.2.1. Circulating pathogens

The circulation of a bacterial pathogen was simulated following the introduction of a single colonized patient in the ICU. The ward was supposed previously free from the studied pathogens, for which we investigated a range of transmissibilities, based on data on MRSA and vancomycin-resistant Enterococci (VRE).

3.2.2. Hygiene Measures: Efficacy and Compliance.

Following patient contacts, HCWs could apply standard hand hygiene procedures, which were 90% efficient at removing transient colonization. From 0 to 5 of all HCWs were supposed noncompliant with hand hygiene recommendations. All possible scenarios were investigated regarding the profile of the noncompliant HCWs among the staff.

HCWs who were fully compliant washed their hands following every patient contact. Those who were not compliant never washed their hands.

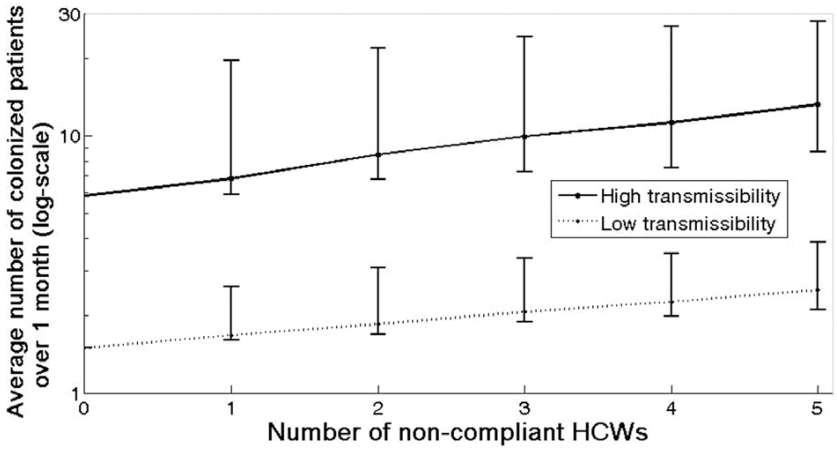

Fig. 2. Total number of patients colonized over 1 month following a single index case (on a log-scale), as a function of the number of noncompliant HCWs. A range of transmissibilities are investigated for the pathogen, from low (dotted line) to high (full line). Lines provide the mean of outbreak sizes computed for all possible scenarios regarding the identity of noncompliant HCWs among the staff. Error bars provide the minimum and maximum among these outbreak sizes.

3.3. Results

3.3.1. Impact of Noncompliance on Pathogen Transmission.

Fig. 2 provides the predicted total number of colonized patients (outbreak size) over 1 month according to the number of noncompliant HCWs. When all HCWs were compliant, from 1.5 to 5.8 patient cases were predicted over 1 month, depending on pathogen transmissibility. As expected, outbreak size increased with noncompliance; for a single noncompliant HCW, it reached 1.7 to 6.8 patient cases on average over 1 month (a 13 to 17% increase). These results were highly dependent on the profile of the noncompliant HCW, as the increase ranged from 2 to 7% for a noncompliant physician and from 73 to 238% for a noncompliant peripatetic HCW.

3.3.2. Importance of the HCW Profile.

Fig. 3 depicts the predicted outbreak size over 1 month with the hypothesis of a single noncompliant HCW (assigned or peripatetic HCW). The impact of noncompliance was strongest when the peripatetic HCW was noncompliant; the HCW profile was most important for a highly transmissible pathogen. Indeed, the predicted total number of patients colonized over 1 month with the highest investigated transmissibility was approximately 3 times greater with 1 noncompliant peripatetic HCW than with 1 noncompliant assigned HCW (Fig. 3*B*).

3.4. Conclusions

This application shows that systematic noncompliant behavior in a few HCWs may have more impact than a global reduction in compliance in all HCWs. This predicted individual impact should be strongest when the noncompliant individuals are peripatetic HCWs. Peripatetic HCWs appear to have major superspreading potential, especially when the transmitted pathogen is highly epidemic. Our findings may explain several reports of outbreaks that were traced back to peripatetic HCWs [14-16].

Peripatetic HCWs, which we defined as HCWs who pay a single (possibly short) visit to all patients in the ICU daily, can be found among many professions represented in ICUs. Some examples are radiologists and physical therapists or other therapists but also physicians on night duty, staff heads, and so on. What is more, it should be

noted that in conditions of understaffing or overcrowding of the ward, HCWs who usually belong in the assigned HCW category may also become peripatetic (noncohorted) HCWs.

4. Discussion

In this paper, we present a tool for simulating pathogen transmission in hospitals and evaluating intervention strategies. Through an application example, we show that this tool may prove useful for addressing important Public Health issues related to the nosocomial risk.

Because it uses the agent-based framework, NosoSim allows the modeling of stochastic events and heterogeneous individual behaviors in a heterogeneously mixed environment. Despite its applicability for the problem at hand, however, agent-based modeling still has some drawbacks. In particular, since it describes the system at the level of its constituent units but not at the top level, its computational demand (at medically relevant scales in terms of simulation durations, number of rooms, etc.) is significant. For instance, performing 1000 simulations of the circulation of two strains in competition in an 18-bed ”corridor-type” ICU (application 1) may take up to 12 minutes with NosoSim running on an Intel Core Duo 2GHz processor.

We developed NosoSim to be flexible, in the sense that modifying and/or adding to any aspect of the simulated hospital ward, human and bacterial agents, should be straightforward. Nevertheless, some actions, such as defining and using a new geographical description for the hospital ward, still necessitate direct modifications in the core Java classes of the program. This should be ameliorated in future versions of NosoSim; a graphical interface allowing to “draw” directly the new hospital ward is planned among further developments.

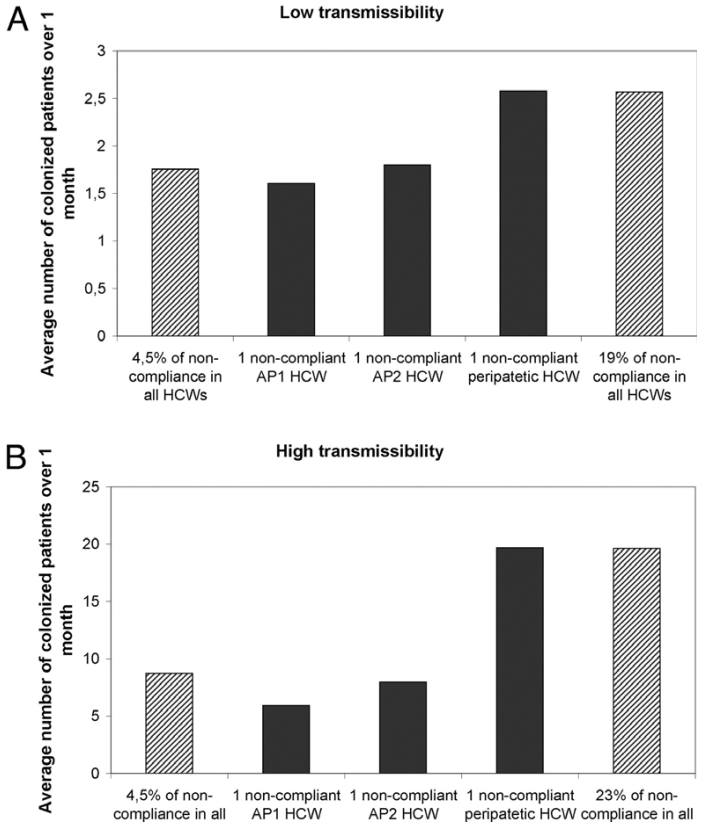

Fig. 3. Total number of patients colonized over 1 month following a single index case, (*A*) for a low-transmissibility pathogen and (*B*) for a high-transmissibility pathogen, in the hypothesis of a single noncompliant HCW: assigned HCW (nurse or physician) or peripatetic HCW.

Future versions should also feature more realistic modeling regarding several aspects which are overly simplified here. This includes interactions (and possible pathogen transmission) between HCWs; interactions of patients and HCWs with the outside world; pathogen transmission through the environment (bedside rails, blood pressure cuffs, etc.) and airborne pathogen transmission.

We are also planning on offering a wider array of interventions that may easily be used (and parameterized) during simulations. Possible interventions include: systematic detection of individuals colonized with a list of pathogens at arrival; periodic surveillance of colonization among patients; use of 1 or several isolation rooms for colonized patients.

Finally, we endeavor to add as many bacterial pathogens and antibiotics to the corresponding built-in libraries as possible, so that NosoSim users need simply select them rather than having to re-define all of their properties. We also plan on using NosoSim to investigate the dynamics of viral pathogens that circulate in hospitals, such as SARS or influenza.

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